Comparison of cathodal, anodal, and bipolar strength-interval curves with temporary and permanent pacing electrodes¹

RAHUL MEHRA AND SEYMOUR FURMAN

From the Cardiothoracic Service, Division of Surgery, Montefiore Hospital and Medical Center, Bronx, New York, USA

SUMMARY Acute animal experiments indicate that ventricular vulnerability to fibrillation or multiple premature contractions is greater during bipolar or anodal stimulation than with unipolar cathodal (with electrodes of equal cathodal and anodal surface area) because the anodal and bipolar absolute refractory periods are shorter, enabling easier excitation in the vulnerable period. To compare the relative safety of stimulation with various commercial electrodes, strength-interval curves were determined in patients during the initial period after electrode implantation (acute studies) and after a few years of pacing (chronic studies). In 9 of 10 acute studies in patients with permanent bipolar electrodes (anode surface area 4.4 times cathode) and in 9 of 10 chronic studies in patients with bipolar electrodes, the unipolar cathodal and bipolar refractory periods were equal. However, in 7 of 12 patients with temporary bipolar electrodes (equal anodal and cathodal surface areas) and in 2 out of 20 acute and chronic studies in patients with permanent bipolar electrodes, the bipolar refractory periods were significantly shorter than cathodal because of anodal stimulation at the proximal electrode. Under appropriate physiological conditions and competitive pacing, these patients would be more vulnerable to arrhythmias with bipolar stimulation than with unipolar cathodal. To decrease that risk, the anodal surface area should be 5 to 7 times the cathodal, or the anode should be removed from the ventricle, especially for temporary pacing in circumstances of high vulnerability to arrhythmias.

Arrhythmias initiated by electrical stimulation of the heart have been well documented in animals and in man (Wiggers and Wegria, 1940; Brooks *et al.*, 1955; Bilitch *et al.*, 1967). The probability of occurrence of pacemaker induced ventricular fibrillation or tachycardia is small but increases in the presence of specific physiological and pharmacological factors and during stimulation about the T wave and in patients with bipolar as compared with unipolar electrodes (Preston, 1973). The electrophysiological basis for the differences in arrhythmia susceptibility with unipolar cathodal, unipolar anodal, and bipolar stimulation has been shown in animals to result from the dissimilarities in the maximum prematurity of stimulation that can occur (Mehra *et al.*, 1977). In an acutely ischaemic ventricle, the vulnerable period for fibrillation or multiple premature contractions

starts at the end of the absolute refractory period and ends at a certain time thereafter. As the refractory periods with anodal and bipolar stimulation are shorter than with cathodal (when equal surface area cathode and anode are used), a response is possible earlier in the cardiac cycle with anodal or bipolar stimuli and their vulnerable periods are, therefore, longer.

In the present study, we evaluate the possible clinical differences between cathodal and bipolar stimulation in relation to ventricular vulnerability. Despite the prevalence of non-competitive pacing, circumstances arise because of pacemaker malfunction or during acute myocardial infarction (Chatterjee *et al.*, 1970) when competition between pacemaker stimuli and spontaneous cardiac rhythm occurs.

To compare the maximum prematurity of stimulation possible with unipolar cathodal, unipolar anodal and bipolar stimuli, the cardiac excitation threshold was measured during the cardiac cycle,

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and strength-interval curves were plotted, in patients with intracardiac electrodes. Two studies were undertaken. In the first, unipolar cathodal and anodal strength-interval curves were compared. Though unipolar anodal stimulation is not used clinically, these data helped to explain the effect of the inadvertent unipolar anodal stimulation that can occur during temporary pacing. In the second study, bipolar and unipolar strength-interval curves were compared.

Patients and methods

Strength-interval curves were derived for different modes of stimulation (Fig. 1) in 43 paced patients. Informed consent was obtained from all patients. Extremely sick patients and those suffering from acute myocardial infarction were excluded from the study. The 'acute studies' were performed with implantable (permanent) electrodes at the time of insertion and with 'temporary' electrodes at insertion or within a few days thereafter. The 'chronic studies' were made on patients with electrodes in use for between 1 and 5 years, during pulse-generator replacement. The electrodes were

either unipolar or bipolar and differed in the stimulating surface areas (Table 1). During unipolar stimulation with an implantable electrode, the subcutaneous pulse generator site was used for the indifferent electrode while for the temporary electrodes, a surgical steel wire inserted in the skin of the right pectoral region acted as the indifferent electrode.

Most patients were paced at 80 beats/minute via their right ventricular electrodes. In some the pacing rate was 90 to 100 beats per minute to eliminate competition. Cathodal pacing at twice the current excitation threshold was used for all studies with the test pulse occurring every seventh beat. From the normally excitable period, the test pulse delay was progressively shortened in 20 ms steps and at each stimulus interval the cathodal, anodal, or bipolar threshold of excitation was measured to an accuracy of 0.1 mA. As the stimulation threshold rose during the relative refractory period, steps of 10 ms duration or less were used. To measure threshold, the test pulse was progressively decreased in amplitude with two applications of the test pulse at each current. Threshold was the minimum test current which, during each of its two applications, resulted in a captured beat. The stimulator¹ delivered constant current pulses of 1.0 ms duration with a maximum output of 9 mA. Resuscitation equipment was always kept available in case of any serious arrhythmias.

Results

(a) UNIPOLAR CATHODAL AND ANODAL STRENGTH-INTERVAL CURVES

Unipolar cathodal and anodal strength-interval curves were plotted in 8 acute and 9 chronic cases (Fig. 2 and 3). In the acute studies, the refractory periods for anodal stimulation were usually shorter than for cathodal at most stimulus currents, while in the chronic studies the anodal refractory periods were usually longer. However, in one acute study, the cathodal refractory period was shorter than anodal at lower stimulus currents (Fig. 2b), and in 2 chronic studies, the anodal refractory periods became shorter at higher stimulus currents (Fig. 3b). In both acute and chronic studies, the mean difference in refractory periods was expressed as a function of current density rather than stimulus current so that it was possible to compare electrodes of different surface area (Table 2). In the acute studies the difference in refractory periods averaged 7 to 9 milliseconds at most current densities. In the chronic studies the anodal refrac-

Fig. 1 Different modes of stimulation for which the strength-interval curves were determined with unipolar and bipolar electrodes.

¹Devices Sales Ltd, Hertfordshire, England

Table 1a *Electrodes used for determining unipolar distal cathodal and anodal strength-interval curves*

	Manufacturer	Electrode type	Distal area (mm ²)	No. of cases
(1) Acute	Medtronic*	6907	11	5
	Medtronic	6901	11	3
				8
(2) Chronic	Cordis†	2mm	12	5
	Medtronic	6901	11	1
	Medtronic	5819	11	1
	Cordis	4mm	28	1
	Medtronic	5816	85	1
				9

Table 1b *Electrodes used for determining bipolar, unipolar distal cathodal, and unipolar proximal anodal strength-interval curves*

	Manufacturer	Electrode type	Distal area (mm ²)	Proximal area (mm ²)	No. of cases
(1) Acute	Medtronic	6901	11	48	10
	Cordis	Temp.	12.5	12.5	12
					22
(2) Chronic	Medtronic	6901	11	48	5
	Medtronic	5819	11	48	1
	GE‡	A2070	11	43	2
	Medtronic	5816	85	80	2
					10

* Medtronic Inc., Minneapolis, Minn.

† Cordis Corp., Miami, Florida

‡ General Electric Co., Milwaukee, Wisconsin

(a) Typical unipolar cathodal and anodal strength-interval curves obtained during an acute study in a patient with a unipolar electrode (Medtronic 6907; surface area 11 mm²). The ordinate represents the excitation current threshold in milliamperes and the abscissa the delay of the test stimulus as measured from the heart rate determining stimulus. Note that the anodal refractory periods are shorter than cathodal for most stimulus currents. (b) Atypical unipolar cathodal and anodal strength-interval curves obtained during an acute study on a patient with a 6097 electrode.

(a) Fig. 3 (a) Typical unipolar cathodal and anodal strength-interval curves obtained during a chronic study in a patient with a 33-month-old unipolar electrode (2 mm electrode; surface area = 12 mm²). Note the longer anodal refractory periods. (b) Atypical unipolar cathodal and anodal strength-interval curves obtained during a chronic study with a 2 mm electrode.

Table 2 Difference between unipolar cathodal and anodal refractory periods (ΔRP) determined in acute and chronic studies

No. of cases		Area (mm ²)		Current density (mA/cm ²)					
				20	30	40	50	60	70
(A) <i>Acute</i>		11	Δ RP (ms)						
8			Mean	4	7	7	9	9	9
			SEM*	2.8	3.5	2.8	1.1	1.1	1.1
(B) <i>Chronic</i>		11, 12	Δ RP (ms)						
8			Mean	-8	-8	-8	-8	-4	-3
			SEM	2.6	2.6	1.9	1.5	3.0	3.8

* SEM = Standard error of the mean.

tory periods were of greater duration than cathodal by an average of 8 to 9 milliseconds. The characteristic 'dip', which represents a narrow region early in the cardiac cycle during which the anodal current threshold is significantly less than in the subsequent interval (Van Dam *et al.*, 1956; Crane-field *et al.*, 1957), was observed in all acute (Fig. 2) and in only 1 of the 9 chronic studies (Fig. 3b).

(b) BIPOLAR AND UNIPOLAR STRENGTH-INTERVAL CURVES

Bipolar, unipolar distal cathodal, and unipolar proximal anodal strength-interval curves were plotted in 22 acute studies. Ten were obtained using the Medtronic model 6901 electrode (tip surface area 11 mm² and proximal 48 mm²) and 12 with the temporary 4F Cordis electrode (proximal and the distal areas equal, each 12.5 mm²). The results from the 2 studies were very

different. With 9 of 10 model 6901 electrodes (90%) the bipolar and unipolar cathodal refractory periods were equal, as the bipolar strength-interval curve was unaffected by proximal anodal stimulation because of its high excitation threshold and therefore followed the lower of the unipolar distal cathodal and proximal anodal strength-interval curves (Fig. 4). In 7 of the 12 cases (58%) with temporary electrodes, the bipolar refractory periods were significantly shorter than unipolar cathodal because of low anodal excitation thresholds at the proximal electrode. Thus, in the case shown in Fig. 5a, at a delay shorter than 285 ms the anodal threshold was lower than the cathodal so that bipolar excitation occurred from the proximal anode to yield equal anodal and bipolar refractory periods. In all 7 cases the 'dip' in the anodal strength-interval curve caused the earlier bipolar excitation, with a 9 ms mean difference between cathodal and bipolar refractory periods at various current densities

Fig. 4 Unipolar distal cathodal, unipolar proximal anodal, and bipolar strength-interval curves obtained during an acute study in a patient with a 6901 bipolar electrode (case 29). Note that the bipolar and unipolar cathodal curves coincide.

(Table 3). With the remaining 5 temporary electrodes (42%), equal duration cathodal and bipolar refractory periods existed up to 9 mA as anodal excitation could not be elicited early in the cardiac cycle (Fig. 5b). The only arrhythmia produced by premature stimulation close to the refractory period was a single unstimulated premature contraction in 2 cases.

In chronic studies with bipolar electrodes, cathodal and bipolar strength-interval curves obtained were similar to those obtained in the acute studies with permanent electrodes. Cathodal and bipolar refractory periods were equal in 9 of the 10 cases (90%) (Fig. 6a). In 7 of the 10 cases, anodal stimulation up to 8 mA did not initiate excitation at the proximal electrode. With only one model 6901 electrode was the bipolar refractory period shorter than the cathodal (Fig. 6b).

Discussion

Animal experiments and clinical experience indicate that the probability of inducing an arrhythmia in a vulnerable myocardium is increased by increasing prematurity of a suprathreshold stimulus (Bilitch *et al.*, 1967; Mehra *et al.*, 1977). The present 'acute' study shows that greater prematurity of stimulation occurs with a bipolar stimulus than with a unipolar cathodal stimulus with temporary

Fig. 5 (a) Unipolar distal cathodal, unipolar proximal anodal, and bipolar strength-interval curves obtained during an acute study in a patient with a temporary bipolar electrode (case 39). The bipolar and unipolar anodal refractory periods are equal and shorter than unipolar cathodal. (b) Strength-interval curves determined with the same electrode in another patient (case 35). In this case stimulation at the proximal anode does not shorten the bipolar refractory period.

Table 3 Difference between cathodal and bipolar refractory periods (ΔRP) determined in patients with temporary electrodes

No. of cases	Distal and proximal area (mm ²)	ΔRP (ms)	Current density (mA/cm ²)					
			20	30	40	50	60	70
7	12.5	Mean	9	9	9	9	9	9
		SD	10	7	5	5	6	6
		SEM	3.8	2.6	1.9	1.8	2.1	2.4

Fig. 6 (a) Typical strength-interval curves obtained during a chronic study in a patient with a 6901 bipolar electrode. Excitation could not be elicited with anodal stimulation from the proximal electrode site. (b) An atypical case with a 6901 electrode (case 11). Note that the bipolar and anodal refractory periods are shorter than cathodal.

electrodes which have equal surface area cathode and anode (each 12.5 mm² in this instance). With such electrodes, shorter bipolar refractory periods were obtained in 7 of 12 cases, as a result of earlier anodal stimulation. In 10 acute and 8 chronic studies with permanent electrodes, in which the anodal surface area was 4 to 4.5 times the cathodal, shorter bipolar refractory periods were observed in only one patient in each group. The difference between temporary and permanent electrodes is statistically significant ($P < 0.05$).

The differences between strength-interval curves of the various bipolar electrodes can be explained on the basis of the strength-interval curves determined with unipolar electrodes. In 7 of 12 cases with temporary bipolar electrodes, anodal and cathodal curves were similar to those obtained with unipolar electrodes. In both, shorter anodal refractory periods and the 'anodal dip' were present. In the others (5 of 12) the anodal refractory periods were longer. This may be the result of a large tissue-electrode separation which can increase the

stimulus current required for threshold, resulting in a shift of the anodal strength-interval curve upward and making the anodal refractory periods longer than cathodal. The longer anodal refractory period found in most acute and chronic studies with permanent electrodes was probably caused by the 4.4 times larger anodal than cathodal surface area. Even when the 2 surface areas were equal in some permanent bipolar electrodes, unipolar chronic strength-interval curves show that the anodal refractory period would still be expected to be longer than the cathodal.

DESIGN OF SAFER PACEMAKER SYSTEMS

The 7 temporary electrodes in which greater prematurity of stimulation occurred with bipolar rather than with cathodal stimulation could be made safer by increasing the duration of the bipolar refractory period so that it is equal to the cathodal. As current density determines excitation threshold (Furman *et al.*, 1975), this can be accomplished by an increase of the anodal surface area. To make

bipolar and cathodal refractory periods equal up to 8 mA of stimulus current the minimum desirable ratio of anodal to cathodal surface area was calculated to be between 1.6 and 4.2. Another way of avoiding the problem of shorter bipolar refractory periods is to move the anode away from the ventricle (Preston, 1974), but this solution may cause problems related to the position of the indifferent terminal.

In only 2 out of 20 acute and chronic studies with permanent electrodes were the bipolar refractory periods shorter than cathodal. In order to make the refractory periods equal with stimulus currents up to 8 mA in these cases, the anodal surface area would have to be at least 7.0 times the cathodal in an acute study and 6.6 in a chronic study. All these results indicate that an anodal to cathodal surface area ratio of 5 to 7 is desirable for the design of safe temporary and permanent bipolar electrodes.

Other factors also affect the duration of the absolute refractory period and hence the maximum prematurity of a suprathreshold stimulus. Strength-

interval curves indicate that lower current densities and short pulse duration stimuli would decrease the probability of precipitating arrhythmias by increasing the shortest stimulus coupling interval (Brooks *et al.*, 1955). The maximum stimulus prematurity with suprathreshold stimuli is also significantly influenced by the time elapsed since electrode insertion, probably as a result of the development of inexcitable tissue around the electrode, which increases the effective surface area and reduces the current density in the excitable tissue (Roy *et al.*, 1968; Tarjan, 1973; Furman *et al.*, 1975). In our chronic studies, the cathodal refractory periods at 70 mA/cm² and 80 beats/minute were 296 ± 19 ms as opposed to 268 ± 27 ms in acute studies with permanent electrodes ($P < 0.05$).

DOCUMENTED CASES OF VENTRICULAR FIBRILLATION AND TACHYCARDIA

The data presented help to explain the 30 documented (with the onset illustrated) cases of pace-

Table 4 Documented cases of arrhythmias induced by pacemaker stimuli

Case no.	Investigators	Arrhythmia*	Mode†	Electrode data		
				Position‡	Type§	Age¶
1	Bertrand <i>et al.</i> (1967)	VF	B	Epi.	P	1 d††
2	Bilitch <i>et al.</i> (1967)	VF	B	Endo.	T	1 d
3	Burgess <i>et al.</i> (1970)	VF	B**	Endo.	T	4 d
4	Castellanos <i>et al.</i> (1970)	VT	B	Endo.	T	1 d
5	Castellanos <i>et al.</i> (1970)	VT	B	Epi.	P	18 m
6	Castellanos <i>et al.</i> (1970)	VT	B	Endo.	T	1 d
7	Castellanos <i>et al.</i> (1970)	VF	B	Endo.	T	1 d
8	Elmqvist <i>et al.</i> (1963)	VT	B	Epi.	P	1 d
9	Forfang and Lippestad (1971)	VT	B	Endo.	T	1 d
10	Grondin <i>et al.</i> (1967)	VT	B	Epi.	P	11 d
11	Jensen <i>et al.</i> (1966)	VT	B	Endo.	P	1½ m
12	Koch and Wiessmann (1971)	VF	B	Epi.	P	54 m
13	Lanoy and Picart (1973)	VF	B	—	P	20 m
14	Lemberg <i>et al.</i> (1969)	VT	B	Endo.	T	1 d
15	Lemberg <i>et al.</i> (1969)	VT	B	Endo.	—	1 d
16	Lemberg <i>et al.</i> (1969)	VF	—	Endo.	T	1 d
17	Lemberg <i>et al.</i> (1969)	VF	—	Endo.	—	1 d
18	Lemberg <i>et al.</i> (1969)	VT	—	Endo.	—	1 d
19	Lumia and Rios (1973)	VT	B	Endo.	T	1 d
20	Martinoli (1970)	VT	B	Endo.	T	1 d
21	Martinoli (1970)	VT	B	Endo.	T	—
22	Overbeck and Buchner (1965)	VT	B	—	—	—
23	Robinson <i>et al.</i> (1965)	VF	B	Epi.	P	16 m
24	Roth <i>et al.</i> (1971)	VF	B	Endo.	T	1 d
25	Roth <i>et al.</i> (1971)	VT	B	Endo.	T	1 d
26	Tavel and Fisch (1964)	VT	B	Epi.	P	1 d
27	Zipes (1975)	VF	U	—	P	22 m
28	Burchell and Meredith (1969)	VT	—	—	T	1 d
29	Schatz <i>et al.</i> (1975)	VF	B	Endo.	T	1 d
30	Batchelder and Zipes (1975)	VF	—	—	T	—

Key:

* VF, ventricular fibrillation; VT, ventricular tachycardia.

† B, bipolar; U, unipolar cathodal.

‡ Endo., endocardial electrode; Epi., epicardial electrode.

§ P, permanent electrode; T, temporary electrode.

¶ Time since electrode implantation, d: days; m: months

** Personal communication.

†† 1 d indicates less than or equal to 1 day.

maker induced ventricular tachycardia or fibrillation. The electrode type was mentioned in 25 of these 30 cases, and was bipolar in all except one (Table 4). It is quite likely that these are only a small portion of the total number of such occurrences. Of the 25 episodes, 13 occurred with temporary endocardial electrodes, almost all of which have equal area cathode and anode. Temporary electrodes are commonly used during acute myocardial infarction, but even in these patients use of the bipolar rather than the unipolar mode of stimulation may have been the important factor in inducing arrhythmias. The possible role of bipolar pacing is further emphasised as 8 of 10 cases of ventricular fibrillation/tachycardia with permanent pacemakers occurred with epicardial electrodes with equal area cathode and anode. Of the remaining 2, 1 occurred with a unipolar cathodal and the other with a bipolar endocardial electrode. In all the documented cases, a pacemaker stimulus from an asynchronous or a malfunctioning demand pacemaker initiated the arrhythmia when it fell on the T wave of an intrinsic beat. Another potentially dangerous situation can arise when a demand pacemaker is switched on. The first stimulus (which in many models does not follow a sensed cardiac cycle) may inadvertently fall within the vulnerable period and precipitate arrhythmias as in cases 19, 28, and 29 (Table 4).

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Requests for reprints to Dr Seymour Furman, Cardiothoracic Service, Division of Surgery, Montefiore Hospital and Medical Center, Bronx, New York 10467, USA.